

Claims

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1. A method for detecting a nucleic acid fragment and/or PNA fragment having a mutation, which comprises
(A) a step of hybridizing at least one fragment among one or more fragments fixed on a substrate, which fragments are selected from the group consisting of one or more nucleic acid fragments and one or more PNA fragments, with at least one fragment of which mutation is to be assayed, which fragment is selected from the group consisting of one or more nucleic acid fragments and one or more PNA fragments;
(B) a step of binding a labeled substance, which is a substance specifically binding to a mismatched base pair, to a mismatched base pair occurring between the hybridized fragments; and
(C) a step of identifying a fragment bound by the substance by detecting the label.

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2. The method of claim 1, wherein the substance specifically binding to a mismatched base pair is a mismatch binding protein.

3. The method of claim 2, wherein the mismatch binding protein is Mut S protein or analogue thereof, or a C/C mismatch binding protein.

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4. ~~The method of claim 1, wherein the substance specifically binding to a mismatched base pair is labeled with at least one kind of substance selected from the group consisting of luminescent proteins, phosphorescent proteins, fluorescent proteins, luminescent substances, fluorescent substances, phosphorescent substances, radioactive substances, stable isotopes, antibodies, antigens, enzymes and proteins.~~

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5. ~~The method of claim 1, wherein the substance specifically binding to a mismatched base pair is labeled with GFP (Green Fluorescence Protein).~~

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6. ~~The method of claim 1, wherein identification and quantification of the fragment having a mismatched base pair are performed~~

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cont. by introducing a label into a nucleic acid and/or PNA fragment to be assayed for mutations, and detecting the label of the nucleic acid and/or PNA fragment to be assayed for mutations.

pat 64/7. The method of claim 6, wherein the label introduced into the nucleic acid and/or PNA fragment to be assayed for mutations produce a signal different from that produced by the label attached to the substance specifically binding to a mismatched base pair, and quantification and identification of the fragment having a mismatched base pair are simultaneously performed.

8. The method of claim 6 or 7, wherein the nucleic acid and/or PNA to be assayed for mutations is labeled with at least one kind of substance selected from the group consisting of luminescent substances, fluorescent substances, phosphorescent substances, stable isotopes, radioactive substances, antibodies, antigens, enzymes and proteins.

9. A method for detecting a nucleic acid fragment and/or PNA fragment having a mutation, which comprises

(A) a step of hybridizing at least one fragment among one or more fragments fixed on a substrate, which fragments are selected from the group consisting of one or more nucleic acid fragments and one or more PNA fragments, with at least one fragment of which mutation is to be assayed, which fragment is selected from the group consisting of one or more nucleic acid fragments and one or more PNA fragments;

(D) a step of treating a mismatched base pair occurring between the hybridized fragments with a substance specifically recognizing and cleaving the mismatched base pair to cut the hybridized fragments at the mismatched base pair, or to remove at least a part of one strand of the fragments hybridized from the mismatched base pair;

(E) a step of labeling a fragment remained on the substrate after the cleavage or the removal; and

(F) a step of identifying the labeled fragment by detecting the label.

10. The method of claim 9, wherein 3' ends of the fragments fixed on the

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Pat → substrate are blocked, and the labeling of the fragment in step (E) is performed by 3' end addition reaction.

11. ~~The method of claim 9 or 10, wherein the substance specifically recognizing and cleaving the mismatched base pair is a nuclease.~~

12. The method of claim 11, wherein the nuclease is S1 nuclease, Mung bean nuclease or RNase H.

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a → 13. ^{claim 9} The method of ~~any one of claims 9-12~~, wherein the labeling of the fragment in the step (E) is performed by an enzyme reaction utilizing a labeled substrate.

14. The method of claim 13, wherein the enzyme reaction is polymerase reaction, kination reaction, ligation reaction, or 3' end addition reaction.

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a → 15. ~~The method of claim 13 or 14, wherein the substrate is labeled with at least one kind of substance selected from the group consisting of luminescent substances, fluorescent substances, phosphorescent substances, stable isotopes, radioactive substances, antibodies, antigens, enzymes and proteins.~~

16. ^{claim 9} The method of ~~any one of claims 9-15~~, wherein detection and quantification of the fragment having a mismatched base pair are performed by introducing a label into a nucleic acid and/or PNA fragment to be assayed for mutations, and detecting the label of the nucleic acid and/or PNA fragment to be assayed for mutations.

17. The method of claim 16, wherein the label introduced into the nucleic acid and/or PNA fragment to be assayed for mutations produce a signal different from that produced by the label attached to the fragment in the step (E), and quantification and identification of the fragment having a mismatched base pair are simultaneously performed.

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a → 18. The method of claim 16 ~~or 17~~, wherein the nucleic acid and/or PNA to

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 be assayed for mutations is labeled with at least one kind of substance selected from the group consisting of luminescent substances, fluorescent substances, phosphorescent substances, stable isotopes, radioactive substances, antibodies, antigens, enzymes and proteins.

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 19. The method of ~~any one of claims 1-18~~ ^{claim 1}, wherein the fragments of nucleic acid or PNA fixed on the substrate are bound to the substrate only at their 5' or 3' end.

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 20. The method of ~~any one of claims 1-19~~ ^{claim 1}, wherein the fragments of nucleic acid or PNA fixed on the substrate are fixed on the substrate by covalent bonds.

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 21. The method of ~~any one of claims 1-20~~ ^{claim 1}, wherein the fragments of nucleic acid or PNA fixed on the substrate are fragments having a cDNA sequence.

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 22. The method of ~~any one of claims 1-21~~ ^{claim 1}, wherein the fragments of nucleic acid or PNA fixed on the substrate have a part or all of cDNA sequence of full length gene.

23. A substance specifically bindable to a mismatched base pair characterized in that it is labeled.

24. The substance of claim 23, wherein the substance specifically bindable to a mismatched base pair is a mismatch binding protein.

25. The substance of claim 24, wherein the mismatch binding protein is Mut S protein or analogue thereof, or a C/C mismatch binding protein.

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 26. The substance of ~~any one of claims 23-25~~ ^{claim 23}, wherein the label is GFP (Green Fluorescence Protein).

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 27. The substance of ~~any one of claims 21-26~~ ^{claim 21}, wherein the label is at least one kind of substance selected from the group consisting of luminescent

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139 proteins, phosphorescent proteins, fluorescent proteins, luminescent substances, fluorescent substances, phosphorescent substances, stable isotopes, radioactive substances, antibodies, antigens, enzymes and proteins.

28. An article comprising a substrate having a surface on which one or more kinds of RNA fragments or PNA fragments are fixed in a hybridizable condition.

29. The article of claim 28, wherein the RNA fragments or PNA fragments fixed on the substrate are bound to the substrate only at their 5' or 3' ends.

a 30. The article of claim 28 or 29, wherein the RNA fragments or PNA fragments fixed on the substrate are fixed to the substrate by covalent bonds.

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